Cardiovascular outcomes study to evaluate the potential of aleglitazar to reduce cardiovascular risk in patients with a recent acute coronary syndrome (ACS) event and type 2 diabetes mellitus (T2D)

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To determine whether aleglitazar reduces cardiovasculair mortality and morbidity (defined as non-fatal myocardial infarction (MI) and non-fatal stroke) in patients with a recent ACS event and type 2 diabetes.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON36231

Source
ToetsingOnline

Brief title
Alecardio

Condition

- Myocardial disorders
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Acuut coronair syndroom

Research involving
Human

Sponsors and support

Primary sponsor: Hoffmann-La Roche
Source(s) of monetary or material Support: Hoffmann - La Roche

Intervention

Keyword: Acute coronary syndrome, Aleglitazar, dual PPAR □/□-agonist, Type 2 diabetes mellitus

Outcome measures

Primary outcome

The time to first occurrence of any component of the composite endpoint of

cardiovascular mortality, non-fatal myocardial infarction and non-fatal stroke.

Secondary outcome

Time to first occurrence of:

- a composite with the following components: cardiovascular mortality, nonfatal

MI, hospitalization for biomarker-negative ACS, and non-fatal stroke

- a composite with the following components: all cause mortality, non-fatal MI

and non-fatal stroke

- individual components of the composite endpoints:

- unanticipated coronary revascularization, ie excluding planned before

randomization

Study description

Background summary

ACS has a high incidence and the high rate of recurrent events in the months

following the initial event. There are approximately 1.5 million admissions to hospital for ACS per year in the US. CHD is a major contributor to mortality, affecting individuals of all ethnic and sociological backgrounds. It is well established that patients with type 2 diabetes have an increased cardiovasculair risk compaired with non-diabetic patients. Patients with CHD and diabetes are at particularly high risk of future recurrent events and their overall prognosis after ACS is much worse compared to patients without diabetes. A subgroup analysis of the PROVE_IT trial in post-ACS patients comparing diabetic patients with non-diabetic patients showed that similar to non-diabetic patients, patients with diabetes following an ACS benefit from early and aggressive treatment with statins. Nevertheless, event rates in post-ACS patients with diabetes remain higher than in post-ACS patients without diabetes. The lipid profile of patients with type 2 diabetes is typically characterized by high levels of triglycerides and low concentrations of HDL-C. this specific lipid profile are associated with higher cardiovascular risk.
Thus patients with diabetes may particularly benefit from a drug that has an effect on these two parameters. Epidemiological data indicate that the prevalence of type 2 diabetes is increasing, making the development of new therapies even more urgent. Taken together, these data demonstrate the high need for new treatments for the reduction of morbidity and mortality in patients with type 2 diabetes after an ACS event. The cardiovascular risk for recurrent events remains unacceptably high, and there is an unmet medical need in these patients.

Study objective

To determine whether aleglitazar reduces cardiovasculair mortality and morbidity (defined as non-fatal myocardial infarction (MI) and non-fatal stroke) in patients with a recent ACS event and type 2 diabetes.

Study design

Multicenter, randomized, double-blind, parallel group, placebocontrolled study

This is a multicenter, randomized, double-blind, parallel group, placebo-controlled study
in T2D patients recently hospitalized for an ACS event. Patients will be treated with
either 150 *g of aleglitazar or matching placebo on top of standard of care for ACS and
T2D.
The study is an event-driven trial and will last until 950 adjudicated events occur
However, no randomized patient will be treated for less than 2.5 years, unless the patient
is prematurely withdrawn from treatment.

The study consists of 3 phases:
1. Screening/ run in period:
Patient screening may begin in the hospital and will continue upon release from the
hospital. Potentially eligible patients will enter a run-in period to allow patients to
stabilize and to complete their planned revascularization procedures. Randomization
should occur when the patient's conditions are deemed stable by the investigator but no later than 8 weeks from this new event. However, for these patients, the allowed maximum duration from index event to randomization is 12 weeks.

2. Double-blind treatment period:
The estimated duration of the treatment period will be between a minimum of 2.5 and 5
years depending on the length of the recruitment period and the primary event rates. The
study medications will be given as fixed doses. During the double blind treatment period,
patients will visit the clinic at month 1, 3, 6, 9 and 12 after randomization. During the
remaining years, patients will visit the clinic every 6 months with phone visits in between
such that there is regular contact every 3 months between the investigator and the patient.

3. Follow-up period:
A safety follow-up visit will take place 4 weeks after the last dose of study medication.

Intervention

Study drug (active or placebo) will be added to a background of contemporary, evidence-based medical care for ACS and CHD risk factors, including diabetes.

Study burden and risks

Patients will have to visit the clinic for 9 times during the 1,5 year. After this every 6 months a visit to the clinic is planned and between these 6 months a telephone call wil be taken place. This will continue untill the "end of treatment" visit. A month afther this visit a follow up visit will take place. During the visits in the first 1,5 year a number of 8 blood withdrawels will take place. After this a blood withdrawal wil take place every 6 month visit until the "end of treatment" visit. Afther this visit the last blood withdrawal

will take plase a month later during the follow up visit.

There will be some discomfort during the blood withdrawal en there could be a possible change in the bloodsugar level of type 2 diabetes patients.
Furthermore there are possible side effects known as side affects with pioglitazone, rosiglitazone and fenofibrate and weight gain, heart faillure, swelling of the retina, pain and inflammation of the muscles.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Males or females aged > 18 years
2. Known T2D/ established T2D (confirmed prior to randomization according to the diagnostic criteria section 4.4)

3. Hospitalization for an ACS event and randomization between hospital discharge and 8 weeks after the ACS index event (day of hospitalization). In case of any subsequent ACS event, procedure related MI or coronary bypass surgery occurring during the run-in period, randomization should occur when the patient's conditions are deemed stable by the investigator but no later than 8 weeks from this new event. However, for these patients, the allowed maximum duration from index event to randomization is 12 weeks.
4. Ability and willingness to give written informed consent and to comply with the requirements of the study

Exclusion criteria

1. Concomitant treatment with a thiazolidinedione and/or fibrate
2. Prior intolerance to a thiazolidinedione, and/or fibrate
3. Triglycerides (fasting) > 400 mg/dL (> 4.5 mmol/L)
4. Patients with clinically apparent liver disease, eg, jaundice, chloeastasis, hepatic impairment, active hepatitis or asymptomatic ALT > 3x ULN.
5. Anemia defined as hemoglobin < 10 g/dL (< 100 g/L, 6.21 mmol/L) or hematocrit < 30 %
6. eGFRMDRD < 45 ml/min/1.73m2
7. Symptomatic congestive heart failure classified as NYHA class II-IV at randomization
8. Hospitalization in the 12-month period preceding the index event for a primary diagnosis of heart failure
9. Peripheral edema which in the judgment of the investigator is believed to be clinically severe
10. Systemic corticosteroid therapy for > 2 weeks, within 3 months prior to screening examination.
11. Any serious medical condition that according to the investigator could interfere with the conduct of the study
12. Serious comorbid disease in which the life expectancy of the patient is shorter than the duration of the trial (e.g. acute systemic infection, cancer or other serious illnesses). Treated basal-cell carcinoma before randomization is not excluded.
13. Unwillingness or inability to comply with study requirements (including subjects whose cooperation is doubtful due to drug abuse or alcohol dependency)
14. Positive pregnancy test, breast feeding women or women of childbearing potential not using highly effective methods of contraception
15. Participation in any clinical trial with an investigational drug or device within one month prior to the screening

Study design

Design

Study phase: 3

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-02-2010
Enrollment:	150
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	N.v.t.
Generic name:	Aleglitazar

Ethics review

Approved WMO Date:	15-12-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-06-2010

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-10-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-10-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-05-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-09-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-07-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-04-2013

Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	BC22140
EudraCT	EUCTR2009-012269-71-NL
CCMO	NL29471.018.09